

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appln. No. 10/662,358

Q77446

**REMARKS**

Claims 6-14 are currently pending.

Claims 1-5 have been canceled. Claim 6 has been amended to place it in independent format by incorporating subject matter of claims from which it depended. Claims 7-10 have been amended to place them more fully in U.S. format.

Claims 11-14 have been added to more fully define the subject matter of the present invention. Support for Claim 11 can be found in the disclosure at, for example, page 4, lines 10-11 of the specification. Support for Claim 12 can be found in the disclosure at, for example, page 8, line 1 - page 9, line 6. Support for Claim 13 can be found at, for example, page 3 lines 11-16. Support for Claim 14 can be found at, for example, page 4, lines 8-9.

No new matter has been added. Entry of the amendment is respectfully requested.

**I. Formal Matter**

Applicants filed an Information Disclosure Statement (IDS) in this application on September 16, 2003. As the Examiner has not yet returned a signed and initialed copy of the Form PTO/SB/08 which accompanied the IDS, Applicants now respectfully request that the Examiner return an acknowledged copy of the Form in her next correspondence.

**II. Objections to the Specification and Claims**

A. At paragraph 3.1 of the Office Action, the Examiner objects to the specification for not containing a reference to the foreign priority document in the first sentence. Applicants respectfully submit that there is no requirement that the specification contain such a reference. However, to advance the prosecution of the application, Applicants include the requested amendment to the specification in the instant Amendment.

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appl. No. 10/662,358

Q77446

The Examiner also objects to the specification, and particularly the second paragraph on page 1, for allegedly using improper English grammar. Included herewith is an amendment to the noted paragraph, such that the paragraph is now grammatically correct.

**B.** At paragraph 3.2 of the Office Action, the Examiner objects to Claim 7 because the Examiner believes that the phrase "a synthase gene is cloned into a chromosome," should read "a synthase gene is integrated into a chromosome." Included herewith is an amendment to Claim 7 in the manner proposed by the Examiner.

In view of the amendments to the specification and claims, Applicants respectfully request reconsideration and withdrawal of these objections.

### **III. Claim Rejections - 35 U.S.C. § 102(b)**

At paragraph 4.1 of the Office Action, Claims 1-3 and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Ferrandez et al. (*J. Biol. Chem.* 1998).

Included herewith is an amendment canceling Claims 1-3 and 5, thus making this rejection moot.

In view of the amendment to the claims, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **IV. Claim Rejections - 35 U.S.C. § 103(a)**

At paragraph 4.3 of the Office Action, Claims 6-10 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ferrandez in view of Tsuge (*FEMS Micro. Letters*, 1999).

The Examiner states that Ferrandez teaches the *maoC* gene of *E. coli* (SEQ ID NO:2). The Examiner admits that Ferrandez does not teach the production of MCL-PHA.

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appln. No. 10/662,358

Q77446

However, the Examiner contends that Tsuge teaches production of MCL-PHA in *E. coli* harboring the *A. caviae* phaC<sub>Ac</sub> gene (encoding a PHA synthase), the *Pseudomonas aeruginosa* phaJ2<sub>Pa</sub> gene (encoding an enoyl-CoA hydratase), and a *fadB* gene deletion.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art to replace the *P. aeruginosa* phaJ2<sub>Pa</sub> gene taught by Tsuge with the *E. coli* maoC gene taught by Ferrandez. The Examiner believes that it would have been obvious to use such a transformant for producing MCL-PHA. The Examiner states that there would have been a high expectation of success given the routine character of genetic manipulations in *E. coli*, and that the motivation to replace the *Pseudomonas* gene with one from *E. coli* would have been a desire to obtain a more efficient producer of MCL-PHA. The Examiner contends that the skilled artisan would have realized that expression of an *E. coli* gene in *E. coli* would be more efficient than expression of a *Pseudomonas* gene in *E. coli*, resulting in more efficient MCL-PHA production.

Applicants respectfully assert that the Examiner has not established a *prima facie* case of obviousness of the rejected claims. In order for the Examiner to maintain a rejection under 35 U.S.C. §103, the Examiner must establish (1) that there is a suggestion or motivation in the cited references to modify the references to make the claimed invention, (2) that there is a reasonable expectation of success that the modification will yield the claimed subject matter, and (3) that the references, as modified, teach all of the claim elements.

In particular, the combined references do not teach at least two elements recited in the claims. First, in contrast to the Examiner's position, Tsuge does not teach the use of *E. coli* having a *fadB* gene deletion. Tsuge merely teaches PHA production in *E. coli* strain LS5218, and as noted at paragraph 2.3 of the article and Table I, this strain has the genotype *fadR601* and

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appln. No. 10/662,358

Q77446

*atoC2(Con)* which only relates to properties of the bacteria concerning fatty acid and PHA metabolism (see the footnote to Table 1). Nor does Ferrandez teach the use of *E. coli* which have a *fadB* gene deletion.

Second, in contrast to the Examiner's statement, the *Pseudomonas aeruginosa* *phaJ2<sub>Pa</sub>* gene of Tsuge and the *paaZ/maoC* gene taught by Ferrandez are not equivalents. The two genes are not known in the art to have substantially the same activity with respect to PHA production. In particular, MCL-PHA produced according to Tsuge's method consists primarily of monomers having 6 carbon atoms. In contrast, MCL-PHA produced using the microorganisms now being claimed consists of monomers with 6-10 carbon atoms (3HHx, 3HO and 3HD), and particularly contains a large amount of monomers with 8-10 carbon atoms (3HO and 3HD) (see page 14, lines 17-24, of the specification for support in this regard). Furthermore, the activity of the *maoC* gene with respect to PHA production in *E. coli* with a *fadB* deletion is novel, so it cannot be said that it would have been obvious to substitute the *paaZ/maoC* gene for the *Pseudomonas aeruginosa* *phaJ2<sub>Pa</sub>* gene.

Moreover, Applicants note that a *prima facie* case of obviousness may be rebutted by a showing of unexpectedly superior results obtained using the claimed invention compared to the closest prior art which is commensurate with the claims. As shown in Example 2 of the specification, the microorganisms of the pending claims produced MCL-PHA at a much higher concentration (44.6%) compared to known microorganism (14%, 21.1% and 29%) (see page 14, lines 7-16, in particular). This is an increase of up to 65% over known microorganism. Such an increase would clearly have been unexpected given that one hydratase is being exchanged for another.

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appln. No. 10/662,358

Q77446

Applicants note that Claims 9 and 10 are directed to a method for producing MCL-PHA using the non-obvious microorganism according to Claims 6 to 8, and to MCL-PHA produced by the method, respectively. As a result, Claims 9 and 10 are also non-obvious.

Claims 11-14 are dependent from Claim 6 and further define the microorganism of Claim 6. As Claim 6 is patentable over cited references, Claims 11-14 are also patentable.

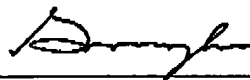
As a result, the combination of Ferrandez and Tsuge does not teach each and every element of the claimed invention, and Applicants respectfully request reconsideration and withdrawal of the rejection.

#### IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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